PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 25 April 2001 (25.04.01)	
International application No. PCT/US00/22158	**Applicant's or agent's file reference** 038602/0162
International filing date (day/month/year) 11 August 2000 (11.08.00)	**Priority date** (day/month/year) 13 August 1999 (13.08.99)
Applicant PLOWMAN, Gregory, D. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

13 March 2001 (13.03.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer S. Mafla
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

12

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
038602/0162		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/22158	11/08/2000	13/08/1999
International Patent Classification (IPC) or national classification and IPC C12N15/55		
Applicant SUGEN, INC. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 23 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☒ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☒ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13/03/2001	19.12.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Morawetz, R Telephone No. +49 89 2399 8155

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/22158

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-112 as originally filed

Claims, No.:

1-23 as originally filed

Drawings, sheets:

1/17-17/17 as originally filed

Sequence listing part of the description, pages:

1-34, filed with the letter of 2.1.2001

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

☐ the description, pages:

☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:
see separate sheet

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

☐ copy of the earlier application whose priority has been claimed.

☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-12, 18-23 (all partially); 13-17 (all completely) .

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-12, 18-23 (all partially); 13-17 (all completely) .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

☐ restricted the claims.

☒ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

☐ complied with.

☐ not complied with for the following reasons:

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

☐ all parts.

☒ the parts relating to claims Nos. 1-12, 18-23 (all partially, insofar related to inventions 1, 6, 9, 10, 14, 20).

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1(partially), 2, 5-12, 18-23
	No:	Claims	1(partially), 3, 4

Inventive step (IS)	Yes:	Claims	
	No:	Claims	1(partially), 2, 5-12, 18-23
Industrial applicability (IA)	Yes:	Claims	1-12, 18-23
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item I
Basis of the report

1. Any sequence listing not contained in the international application as filed shall not, subject to Article 34, form part of the international application (Rule 13ter.1(f) PCT).

2. The numbering of the sequences of the sequence listing filed with letter dated 2.1.2001 does not correspond to the original numbering of the sequences causing original SEQ ID NO: 37 to become SEQ ID NO: 35, original SEQ ID NO: 38 to become SEQ ID NO: 36, etc. This has been taken into account when carrying out the search and examination.

Re Item II
Priority

1. This report has been established under the assumption that the entire subject-matter is entitled to the claimed priority. The "P" documents cited in the search report have not been considered for novelty and/or inventive step.

Re Item III
Non-establishment of report with regard to novelty, inventive step and industrial applicability

1. The applicant's attention is drawn to the fact that claims or part of claims, relating to inventions in respect of which no international search report has been established (see form PCT/ISA/210) need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). Claims 13-17 have, consequently, not been examined.

Re Item IV

Lack of unity of invention

1. The International Search Authority considered that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3 PCT).

   The present application provides twenty different putative dual specificity protein phosphatases.

   However, dual specificity protein phosphatases are already known from the prior art (see e.g. WO9902704; Muda, M. et al., (1997) JBC 272(8) pp. 5141-5151).
   The problem underlying the present application can, thus, be seen as the provision of further dual specificity phosphatases.
   The solutions as disclosed and claimed in the present application can be summarised as the provision of the 20 nucleotide sequences and the polypeptides they encode (SEQ ID Nos: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42).
   Due to the fact that dual specificity protein phosphatases are already known from the prior art, due to the essential differences between the primary structures of the 20 sequences claimed and due to the fact that no other technical feature can be distinguished which in light of the prior art could be regarded as a special, common technical feature, this authority is of the opinion that there is no single inventive concept underlying the plurality of different inventions of the present application in the sense of Rule 13.2 PCT.

   The International Search Report covers inventions Nos: 1, 6 and 9-20.

2. The International Preliminary Examining Authority maintained the objection regarding lack of unity of the international application.

3. With telefax of 23.7.2001 the applicant elected further prosecution of inventions: 1, 6, 9, 10, 14 and 20.

Re Item V: Invention 1

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents, the numbering corresponds to the listing of the documents in the international search report:

   D1: DATABASE EMBL [Online] Accession number AI021222, 18.06.1998
   D2: DATABASE SWALL [Online] Accession number O43183, 01.06.1998
   D2': Li, L. et al., JBC (1997) 272, 29403-29406
   D3: DATABASE SWALL [Online] Accession number P91585, 01.05.1997
   D4: MUDA, M. et al., JBC (1997) 272, 5141-5151
   D5: DATABASE EMBL [Online] Accession number AA023073, 10.08.1996
   D6: DATABASE EMBL [Online] Accession number AA028820, 17.08.1996

2. The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1 (c)-(i) and 3 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

   Present application provides 20 different putative dual specificity protein phosphatases, identified through the use of a motif extraction bioinformatics script. Invention 1 relates to a partial murine phosphatase characterized by SEQ ID NO:2. According to the description (page 33, line 14-20; page 35, lines 6-14) the phosphatase belongs to the Cdc14 family of dual- specificity phosphatases. Present application does not provide any experimental evidence of the expression of the putatively encoded polypeptide or of its biological role, e.g. its substrates.

2.1. The subject-matter of claims 1 (c)-(e) and 3 is considered anticipated by D1.

   D1 discloses the sequence of a murine cDNA clone which shows 97.4 % identity in 456 nt overlap (235-690:1-453) with SEQ ID NO:1. The polypeptide encoded by the sequence of D1 shows 96% identity in 76 aa overlap with SEQ ID NO:2 (75-150:1-226). D1 also mentions the similarity of the sequence with the phosphatase of D3.

2.2. The subject-matter of claims 1 (c)-(i) and 3 is considered anticipated by both D5 and D6.

D5 discloses the sequence of a murine cDNA clone which shows 99.6% identity in 476 nt overlap (1-476:15-489) with SEQ ID NO:1. The polypeptide encoded by the sequence of D5 shows 100% identity in 117 aa overlap with SEQ ID NO:2 (1-119:10-127).

D6 discloses the sequence of a murine cDNA clone which shows 100% identity in 349 nt overlap (1-349:50-398) with SEQ ID NO:1. The polypeptide encoded by the sequence of D6 shows 100% identity in 112 aa overlap with SEQ ID NO:2 (1-112:22-134).

2.3. The subject-matter of claims 1(a), (b), (j), (k), 2, 4-12 and 18-23 appears to be novel in view of the available prior art.

3. The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of claims 1(a), (b), (j), (k), 2, 4-12 and 18-23 does not involve an inventive step as defined in the regulations (Rule 65 (1)-(2) PCT).

3.1. Claim 1 (a) relates to an isolated, enriched or purified nucleic acid molecule encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO: 2. SEQ ID NO:2 encodes a partial putative murine dual-specific phosphatase, which is assumed to belong to the Cdc14 family of dual- specificity phosphatases.

Document D2', which is considered to represent the most relevant state of the art, discloses (abstract) cloning of two human cDNAs encoding proteins which share sequence identity to the yeast CDC14p and show dual specific phosphatase activities.

D4 discloses (abstract; page 5143, left hand column, paragraph 4) identification of MKP-4 by searching the expressed sequence tag data base (dbEST) for sequences similar to dual specificity phosphatases.

The subject-matter of claim 1 (a) differs from the prior art in that it relates to a

nucleic acid molecule encoding an alternative dual-specific phosphatase which, based on similarity with members of the CDC14 family, might be a murine member of the CDC14 family.

Starting from this prior art and depending on whether the dual-specific phosphatase of present invention is defacto a murine member of the CDC14 family two alternative technical problems to be solved by the present invention can be defined, namely 1) the provision of a nucleic acid molecule encoding an alternative murine dual-specific phosphatase and 2) the provision of a nucleic acid molecule encoding a murine member of the CDC14 family.

In neither case can the solution proposed in claim 1 (a) of the present application be considered as involving an inventive step for the following reasons:

Regarding problem 1: Given that D4 clearly teaches how to obtain further dual-specific phosphatases and considering that the dual-specific phosphatase encoded by the nucleic acid molecule of claim 1 (a) was not shown to have any particular technical effect its provision is considered no more that the provision of an arbitrary dual-specific phosphatase out of the hundreds that are available in the murine gene pool. An arbitrary selection from this pool cannot involve an inventive step, because, in order to fulfil the requirements of Article 33 PCT a selection must be justified by a technical purpose, i.e. by a hitherto unknown or unexpected technical effect resulting from those structural features which distinguish the compound claimed from all the other possible solutions. No such technical effect has been disclosed for the dual-specific phosphatase encoded by the nucleic acid molecule of claim 1 (a).

Regarding problem 2: human Cdc14B cDNA and yeast CDC14 were cloned before the priority date of present application (see D2'). The provision of a nucleic acid molecule encoding a murine member of a known family of proteins is considered to lack an inventive step because, at the priority date, considering the teaching of D2', the skilled person could expect to perform the cloning of the murine nucleic acid molecule in a fairly straightforward manner.

3.2. Claims 1 (b) (j) (k), 2, 4-12 and 18-23 concern embodiments which are familiar to

the skilled person. Consequently, they would only be considered inventive if they were based upon a new and inventive dual specificity phosphatase. For the present claims this is not the case. Therefore the subject-matter of these claims is considered to be obvious.

Re Item V: Invention 6

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents, the numbering corresponds to the listing of the documents in the international search report:

   D4: MUDA, M. et al., JBC (1997) 272, 5141-5151
   D7: DATABASE EMBL [Online] Accession number AA374753, 18.04.1997
   D8: DATABASE EMBL [Online] Accession number AA411671, 04.05.1997
   D44: Keyse, S.M., BBA (1995) 1265, 152-160

2. The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1 (c)- (i), 3 and 4 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

   Present application provides 20 different putative dual specificity protein phosphatases, identified through the use of a motif extraction bioinformatics script. Invention 6 relates to a human phosphatase characterized by SEQ ID NO:12. According to the description (page 35, lines 22-27; page 39, lines 22-28) the 184 aa full length protein belongs to the MAP kinase phosphatase (MKP) family of dual-specificity phosphatases. Apart of expression of the putative dual specificity protein phosphatase in a variety of tissues (see Fig. 3), the application does not provide any experimental evidence of the biological role of the phosphatase, e.g. its substrates.

2.1. The subject-matter of claim 1 (c)- (i), 3 and 4 is considered anticipated by D7.

   D7 discloses the sequence of a human cDNA which shows similarity to the human MKP CL100 (see D44). The polypeptide encoded by the sequence of D7 shows

100% identity in 83 aa overlap with SEQ ID NO:12.

2.2. The subject-matter of claim 1 (c)-(e), 3 and 4 is considered anticipated by D8.

D8 discloses the sequence of a human cDNA which shows similarity to dual specificity phosphatase E218398. The polypeptide encoded by the sequence of D8 shows 98.9% identity in 93 aa overlap with SEQ ID NO:12.

2.3. The subject-matter of claims 1(a), (b), (j), (k), 2, 5-12 and 18-23 appears to be novel in view of the available prior art.

3. The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of claims 1(a), (b), (j), (k), 2, 5-12 and 18-23 does not involve an inventive step as defined in the regulations (Rule 65 (1)-(2) PCT).

3.1. Claim 1 (a) relates to an isolated, enriched or purified nucleic acid molecule encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO: 12. SEQ ID NO:12 encodes a putative human dual-specific phosphatase belonging to the family of MKPs.

Document D7, which is considered to represent the most relevant state of the art, discloses the sequence of a human cDNA which shows similarity to the human MKP CL100. The polypeptide encoded by the sequence of D7 shows 100% identity in 83 aa overlap with SEQ ID NO:12.

The subject-matter of claim 1 (a) differs from D7 in that it relates to a nucleic acid molecule encoding the corresponding full length phosphatase.

Starting from this prior art the technical problem to be solved by the present invention can be defined as the cloning of the nucleic acid molecule encoding the full length phosphatase corresponding to the partial clone known from D7.

The solution proposed in claim 1 (a) of the present application cannot be considered as involving an inventive step for the following reasons:

The cloning of a nucleic acid molecule encoding the full length polypeptide of a known partial cDNA clone is considered to lack an inventive step because, at the priority date, the skilled person could expect to perform the cloning of the nucleic acid molecule in a fairly straightforward manner.

This authority is furthermore of the opinion, that in view of the teaching of D4 or D44, the provision of a nucleic acid molecule encoding yet another MKP which was not shown to have any particular technical effect is considered no more that the provision of an arbitrary dual-specific phosphatase out of the hundreds that are available in the human gene pool. An arbitrary selection from this pool cannot involve an inventive step, because, in order to fulfil the requirements of Article 33 PCT a selection must be justified by a technical purpose, i.e. by a hitherto unknown or unexpected technical effect resulting from those structural features which distinguish the compound claimed from all the other possible solutions. No such technical effect has been disclosed for the MKP encoded by the nucleic acid molecule of claim 1 (a).

3.2. Claims 1 (b) (j) (k), 2, 5-12 and 18-23 concern embodiments which are familiar to the skilled person. Consequently, they would only be considered inventive if they were based upon a new and inventive MKP. For the present claims this is not the case. Therefore the subject-matter of these claims is considered to be obvious.

Re Item V: Invention 9

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents, the numbering corresponds to the listing of the documents in the international search report:

   D4: MUDA, M. et al., JBC (1997) 272, 5141-5151
   D9: DATABASE EMBL [Online] Accession number AA461185, 13.06.1997
   D11: DATABASE EMBL [Online] Accession number AA723271, 08.01.1998

2. The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1 (c)-(e), 3 and 4 is not new in respect of

prior art as defined in the regulations (Rule 64(1)-(3) PCT).

Present application provides 20 different putative dual specificity protein phosphatases, identified through the use of a motif extraction bioinformatics script. Invention 9 relates to a human phosphatase characterized by SEQ ID NO:18. According to the description (page 35, lines 22-27; page 39, lines 29 - page 40, line 6) the 198 aa full length protein belongs to the MAP kinase phosphatase (MKP) family of dual-specificity phosphatases and is closely related to the DUS13 protein phosphatase (D53, P doc) with 99% identity over 198 aa. Present application does not provide any experimental evidence of the expression of the putatively encoded polypeptide or of its biological role, e.g. its substrates.

2.1. The subject-matter of claims 1 (c)-(e), 3 and 4 is considered anticipated by D9.

D9 discloses the sequence of a human cDNA clone which shows similarity to tyrosine phosphatase CE00468. The polypeptide encoded by the sequence of D9 shows 98.8% identity in 85 aa overlap with SEQ ID NO:18.

2.2. The subject-matter of claims 1 (c)-(e), 3 and 4 is considered anticipated by D11.

D11 discloses the sequence of a human cDNA clone which shows similarity to dual specificity protein phosphatase 3. The polypeptide encoded by the sequence of D11 shows 94.6% identity in 74 aa overlap with SEQ ID NO:18.

2.3. The subject-matter of claims 1(a), (b), (f) - (k), 2, 5-12 and 18-23 appears to be novel in view of the available prior art.

3. The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of claims 1(a), (b), (f) - (k), 2, 5-12 and 18-23 does not involve an inventive step as defined in the regulations (Rule 65 (1)-(2) PCT).

3.1. Claim 1 (a) relates to an isolated, enriched or purified nucleic acid molecule encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO: 18. SEQ ID NO:18 encodes a putative human MKP.

D4, which is considered to represent the most relevant state of the art, discloses the cloning of a new member of the MKP family, MKP-4.

The subject-matter of claim 1 (a) differs from D4 in that it relates to a nucleic acid molecule encoding an alternative putative MKP.

Starting from this prior art the technical problem to be solved by the present invention can be defined as the cloning of the nucleic acid molecule encoding an alternative MKP.

The solution proposed in claim 1 (a) of the present application cannot be considered as involving an inventive step for the following reasons:

Given that D4 clearly teaches how to obtain further MKPs and considering that the MKP encoded by the nucleic acid molecule of claim 1 (a) was not shown to have any particular technical effect its provision is considered no more that the provision of an arbitrary MKP out of the many that are available in the human gene pool. An arbitrary selection from this pool cannot involve an inventive step, because, in order to fulfil the requirements of Article 33 PCT a selection must be justified by a technical purpose, i.e. by a hitherto unknown or unexpected technical effect resulting from those structural features which distinguish the compound claimed from all the other possible solutions. No such technical effect has been disclosed for the MKP encoded by the nucleic acid molecule of claim 1 (a).

3.2. Claims 1 (b), (f) - (k), 2, 5-12 and 18-23 concern embodiments which are familiar to the skilled person. Consequently, they would only be considered inventive if they were based upon a new and inventive dual specificity phosphatase. For the present claims this is not the case. Therefore the subject-matter of these claims is considered to be obvious.

Re Item V: Invention 10

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents, the numbering corresponds to the listing of the documents in the international search report:

   D4: MUDA, M. et al., JBC (1997) 272, 5141-5151
   D12: DATABASE EMBL [Online] Accession number AA813372, 16.02.1998
   D13: DATABASE EMBL [Online] Accession number AI025489, 19.06.1998
   D43: DATABASE SWALL [Online] Accession number Q93592, 01.02.1997

2. The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1 (c)-(e), 3 and 4 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

   Present application provides 20 different putative dual specificity protein phosphatases, identified through the use of a motif extraction bioinformatics script. Invention 10 relates to a human phosphatase characterized by SEQ ID NO:20. According to the description (page 35, lines 22-27; page 40, lines 26 - page 41, line 2) the 190 aa protein belongs to the MAP kinase phosphatase (MKP) family of dual-specificity phosphatases. Present application does not provide any experimental evidence of the expression of the putatively encoded polypeptide or of its biological role, e.g. its substrates.

2.1. The subject-matter of claim 1 (c)-(e), 3 and 4 is considered anticipated by D12.

   D12 discloses the sequence of a human cDNA clone which shows similarity to the dual-specific phosphatase Q93592 (see D43). The polypeptide encoded by the sequence of D12 shows 97% identity in 101 aa overlap with SEQ ID NO:20.

2.2. The subject-matter of claim 1 (c)-(e), 3 and 4 is considered anticipated by D13.

   D13 discloses the sequence of a human cDNA clone which shows similarity to protein-tyrosine phosphatase CE09669. The polypeptide encoded by the

sequence of D13 shows 99% identity in 102 aa overlap with SEQ ID NO:20.

2.3. The subject-matter of claims 1(a), (b), (f) - (k), 2, 5-12 and 18-23 appears to be novel in view of the available prior art.

3. The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of claims 1(a), (b), (f) - (k), 2, 5-12 and 18-23 does not involve an inventive step as defined in the regulations (Rule 65 (1)-(2) PCT).

3.1. Claim 1 (a) relates to an isolated, enriched or purified nucleic acid molecule encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO: 20. SEQ ID NO:20 encodes a putative human MKP.

D4, which is considered to represent the most relevant state of the art, discloses the cloning of a new member of the MKP family, MKP-4.

The subject-matter of claim 1 (a) differs from D4 in that it relates to a nucleic acid molecule encoding an alternative putative MKP.

Starting from this prior art the technical problem to be solved by the present invention can be defined as the cloning of the nucleic acid molecule encoding an alternative MKP.

The solution proposed in claim 1 (a) of the present application cannot be considered as involving an inventive step and the same argumentation as set out above for invention 9 (item V, 3.1.) applies.

3.2. Claims 1 (b), (f) - (k), 2, 5-12 and 18-23 concern embodiments which are familiar to the skilled person. Consequently, they would only be considered inventive if they were based upon a new and inventive dual specificity phosphatase. For the present claims this is not the case. Therefore the subject-matter of these claims is considered to be obvious.

Re Item V: Invention 14

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents, the numbering corresponds to the listing of the documents in the international search report:

   D23: DATABASE EMBL [Online] Accession number AI025365, 19.06.1998

2. The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1 (c)-(i), 3 and 4 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

   Present application provides 20 different putative dual specificity protein phosphatases, identified through the use of a motif extraction bioinformatics script. Invention 14 relates to a human phosphatase characterized by SEQ ID NO:28. According to the description (page 35, lines 22-27; page 40, lines 7-14) the 217 aa full length human protein belongs to the MAP kinase phosphatase (MKP) family of dual-specificity phosphatases. Appart of expression of the putative dual specificity protein phosphatase in a variety of tissues (see Fig. 3), the application does not provide any experimental evidence of the biological role of the phosphatase, e.g. its substrates.

2.1. The subject-matter of claims 1 (c)-(i), 3 and 4 is considered anticipated by D23.

   D23 discloses the sequence of a human cDNA clone which shows similarity tc dual-specific protein phosphatase 5. The polypeptide encoded by the sequence of D23 shows 100 % identity in 71 aa overlap with SEQ ID NO:28.

2.2. The subject-matter of claims 1(a), (b), (j), (k), 2, 5-12 and 18-23 appears to be novel in view of the available prior art.

3. The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of claims 1(a), (b), (j), (k), 2, 5-12 and 18-23 does not involve an inventive step as defined in the regulations (Rule 65 (1)-(2) PCT).

3.1. Claim 1 (a) relates to an isolated, enriched or purified nucleic acid molecule encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO: 28. SEQ ID NO:28 encodes a putative human dual-specific phosphatase.

D23, which is considered to represent the most relevant state of the art, discloses the sequence of a human cDNA clone which shows similarity to dual-specific protein phosphatase 5. The polypeptide encoded by the sequence of D23 shows 100 % identity in 71 aa overlap with SEQ ID NO:28.

The subject-matter of claim 1 (a) differs from D23 in that it relates to a nucleic acid molecule encoding the corresponding full length phosphatase.

Starting from this prior art the technical problem to be solved by the present invention can be defined as the cloning of the nucleic acid molecule encoding the full length phosphatase corresponding to the partial clone known from D23.

The solution proposed in claim 1 (a) of the present application cannot be considered as involving an inventive step an the same argumentation as set out above for invention 6 (item V, 3.1.) applies.

3.2. Claims 1 (b), (j), (k), 2, 5-12 and 18-23 concern embodiments which are familiar to the skilled person. Consequently, they would only be considered inventive if they were based upon a new and inventive dual specificity phosphatase. For the present claims this is not the case. Therefore the subject-matter of these claims is considered to be obvious.

Re Item V: Invention 20

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents, the numbering corresponds to the listing of the documents in the international search report:

D2': Li, L. et al., JBC (1997) 272, 29403-29406
D3: DATABASE SWALL [Online] Accession number P91585, 01.05.1997

D39: DATABASE EMBL [Online] Accession number AI816223, 12.07.1999

2. The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1 (c)-(e), 3 and 4 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

Present application provides 20 different putative dual specificity protein phosphatases, identified through the use of a motif extraction bioinformatics script. Invention 20 relates to a human phosphatase characterized by SEQ ID NO:42 (=SEQ ID NO:40 of sequence listing submitted with letter dated 2.1.2001) . According to the description (Figure 1) the phosphatase belongs to the Cdc14 family of dual- specificity phosphatases. Present application does not provide any experimental evidence of the expression of the putatively encoded polypeptide or of its biological role, e.g. its substrates.

2.1. The subject-matter of claim 1 (c)-(e), 3 and 4 is considered anticipated by D39.

D39 discloses the sequence of a human cDNA clone which shows similarity to tyrosine phosphatase P91585 (see D3). The polypeptide encoded by the sequence of D39 shows 99.3% identity in 141 aa overlap with SEQ ID NO:40.

2.2. The subject-matter of claims 1(a), (b), (f) - (k), 2, 5-12 and 18-23 appears to be novel in view of the available prior art.

3. The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of claims 1(a), (b), (f) - (k), 2, 5-12 and 18-23 does not involve an inventive step as defined in the regulations (Rule 65 (1)-(2) PCT).

3.1. Claim 1 (a) relates to an isolated, enriched or purified nucleic acid molecule encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO: 40. SEQ ID NO:40 encodes a putative human member of the CDC14 family.

Document D2', which is considered to represent the most relevant state of the art, discloses (abstract) cloning of two human cDNAs encoding proteins which share sequence identity to the yeast CDC14p and show dual specific phosphatase

activities.

The subject-matter of claim 1 (a) differs from the prior art in that it relates to a nucleic acid molecule encoding an alternative dual-specific phosphatase which, based on similarity, might be an additional human member of the CDC14 family.

Starting from this prior art the technical problem to be solved by the present invention can be defined as the cloning of the nucleic acid molecule encoding an alternative human member of the CDC14 family.

The solution proposed in claim 1 (a) of the present application cannot be considered as involving an inventive step for the following reasons:

Given that D2' clearly teaches how to obtain further human dual-specific phosphatases related to yeast CDC14 protein and considering that the dual-specific phosphatase encoded by the nucleic acid molecule of claim 1 (a) was not shown to have any particular technical effect its provision is considered no more that the provision of an arbitrary dual-specific phosphatase out of the many that are available in the human gene pool. An arbitrary selection from this pool cannot involve an inventive step, because, in order to fulfil the requirements of Article 33 PCT a selection must be justified by a technical purpose, i.e. by a hitherto unknown or unexpected technical effect resulting from those structural features which distinguish the compound claimed from all the other possible solutions. No such technical effect has been disclosed for the dual-specific phosphatase encoded by the nucleic acid molecule of claim 1 (a).

3.2. Claims 1 (b), (f) - (k), 2, 5-12 and 18-23 concern embodiments which are familiar to the skilled person. Consequently, they would only be considered inventive if they were based upon a new and inventive dual specificity phosphatase. For the present claims this is not the case. Therefore the subject-matter of these claims is considered to be obvious.

Re Item VI

Certain documents cited

Certain published documents (Rule 70.10)

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO0105983	25.01.2001	19.07.2000	20.07.1999
WO0102581	11.01.2001	20.04.2000	02.07.1999
WO0102582	11.01.2001	29.06.2000	02.07.1999
WO0006728	10.02.2000	28.07.1999	28.07.1998
WO0060098	12.10.2000	07.04.2000	07.04.1999
WO0018890	06.04.2000	30.09.1999	30.09.1998
WO0063393	26.10.2000	19.04.2000	20.04.1999
WO0060099	12.10.2000	07.04.2000	07.04.1999
WO0120004	22.03.2001	14.09.2000	15.09.1999

These documents are not considered part of the prior art for the purpose of Article 33 (2) and (3) PCT.

Re Item VIII

Certain observations on the international application

1. Article 6 PCT and Rule 6 PCT

1.1. Claims 1(d), 1(f), 5, 6 (b), 6(c), 11 (a), 12(a), 18(a) and 21(a) are unclear because they refer to amino acid numbers as set forth by the respective domain delimitations in any of the Figures.

1.2. The scope of claim 1(d) and others insofar referring to nucleic acid molecules encoding polypeptides "lacking one or more, but not all, of the amino acid numbers as set forth by the respective domain delimitations in any of the Figures" (emphasis added) is considered unclear and unduly broad. A nucleic acid

encoding 1 amino acid falls essentially within the scope of these claims. The scope of said claims is furthermore unclear and unduly broad because the claimed molecules do not have to retain any of the properties of the molecule to which they ultimately refer.

1.3. Claims 1 (f), 5, 6 (c), 18 have been interpreted to relate to the full length polypeptides encoded by the SEQ ID NO:s shown in Figure 5.

1.4. Claims 18- 23 are not supported by the description as required by Article 6 PCT, as their scope is broader than justified by the description and drawings. The reasons therefor are the following: the application as originally filed, does not disclose if any of the putative phosphatases is involved in any kind of disease or disorder, let alone in any of the diseases or disorders specifically mentioned in said claims.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
038602/0162		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 00/ 22158	11/08/2000	13/08/1999
Applicant		
SUGEN, INC. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 24 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [X] furnished subsequently to this Authority in written form.

   [X] furnished subsequently to this Authority in computer readble form.

   [X] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [X] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   PROTEIN PHOSPHATASES AND DIAGNOSIS AND TREATMENT OF PHOSPHATASE-RELATED DISORDERS

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. ____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/22158

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [ ] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. [X] Claims Nos.: 13-17
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [X] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

inventions 1, 6, 9-20

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:2 and subject-matter relating thereto.

2. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:4 and subject-matter relating thereto.

3. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:6 and subject-matter relating thereto.

4. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:8 and subject-matter relating thereto.

5. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:10 and subject-matter relating thereto.

6. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:12 and subject-matter relating thereto.

7. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:14 and subject-matter relating thereto.

8. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

sequence set forth in SEQ ID NO:16 and subject-matter relating thereto.

9. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:18 and subject-matter relating thereto.

10. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:20 and subject-matter relating thereto.

11. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:22 and subject-matter relating thereto.

12. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:24 and subject-matter relating thereto.

13. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:26 and subject-matter relating thereto.

14. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:28 and subject-matter relating thereto.

15. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:30 and subject-matter relating thereto.

16. Claims: 1-12, 18-23 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:32 and subject-matter relating thereto.

17. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:34 and subject-matter relating thereto.

18. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:38 and subject-matter relating thereto.

19. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:40 and subject-matter relating thereto.

20. Claims: 1-12, 18-23 (all partially)

A nucleic acid encoding a polypeptide having the amino acid sequence set forth in SEQ ID NO:42 and subject-matter relating thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 13-17

Present claims 13-17 relate to the use of a substance defined by reference to a desirable characteristic or property, namely the ability to modulate the activity of a phosphatase.

The claims cover all methods for treating a disease or disorder involving the use of a substance having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for none of such methods or substances. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.
Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the method by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/22158

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9902704 A	21-01-1999	AU 8479498 A	08-02-1999
WO 0006728 A	10-02-2000	AU 5134999 A	21-02-2000
		EP 1100904 A	23-05-2001
WO 0018890 A	06-04-2000	AU 6410599 A	17-04-2000
WO 0105983 A	25-01-2001	AU 6355700 A	05-02-2001
WO 0102581 A	11-01-2001	AU 4206700 A	23-10-2000
		AU 4367600 A	22-01-2001
		AU 5783800 A	22-01-2001
		WO 0060092 A	12-10-2000
		WO 0102582 A	11-01-2001
WO 0102582 A	11-01-2001	AU 4206700 A	23-10-2000
		AU 4367600 A	22-01-2001
		AU 5783800 A	22-01-2001
		WO 0060092 A	12-10-2000
		WO 0102581 A	11-01-2001
WO 0060098 A	12-10-2000	AU 4210100 A	23-10-2000
WO 0063393 A	26-10-2000	AU 4470200 A	02-11-2000
WO 0056899 A	28-09-2000	AU 4020000 A	09-10-2000
WO 0065069 A	02-11-2000	AU 4683200 A	10-11-2000
WO 0060099 A	12-10-2000	AU 4213100 A	23-10-2000
WO 0055332 A	21-09-2000	AU 3899600 A	04-10-2000
		AU 5034200 A	12-12-2000
		WO 0071679 A	30-11-2000
WO 0065068 A	02-11-2000	AU 4658400 A	10-11-2000
WO 0120004 A	22-03-2001	NONE	

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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EE	Estonia	**LR**	Liberia	**SG**	Singapore		

INTERNATIONAL SEARCH REPORT

Inte ..ional Application No
PCT/US 98/14205

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N15/55 C12N9/16 A61K31/70 C07K16/40 C12Q1/68
G01N33/53 C12Q1/42 A61K38/46

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K A61k C12Q G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	LI, J. ET AL.: "PTEN, a putative tyrosine phosphatase gene mutated in human brain, breast, and prostate cancer." SCIENCE, vol. 275, 28 March 1997, pages 1943-1946, XP002066155 cited in the application see the whole document -& DATABASE EMBL - EMHUM2 Entry HSU93051, Acc.No. U93051, 3 April 1997 LI, J. ET AL.: "Human putative protein tyrosine phosphatase (PTEN) mRNA, complete cds." XP002066159 see the whole document	1-19,22, 23, 25-28,41

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 January 1999	18/01/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax. (+31-70) 340-3016	Smalt, R

4

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/US 98/14205

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 15686 A (IMP CANCER RES TECH ;SPURR NIGEL KAY (GB); GRAY IAN CHRISTOPHER (G) 1 May 1997	1-12,14, 23-25, 27, 36-41,44
Y	see page 26, line 3 - line 6 see page 27, line 30 - page 28, line 5 see page 43, line 14 - page 44, line 4; claims 25,26,28.45,59,63	29-35
X	LI, D-M. ET AL.: "TEP1, encoded by a candidate tumor suppressor locus, is a novel protein tyrosine phosphatase regulated by transforming growth factor beta." CANCER RESEARCH, vol. 57, 1 June 1997, pages 2124-2129, XP002066157	4-12,14, 23
Y	see the whole document	29-35
X	STECK, P.A. ET AL.: "Identification of a candidate tumor suppressor gene at 10q23.3 that is mutated in multiple advanced cancers. MMAC1." NATURE GENETICS, vol. 15, April 1997, pages 356-363. XP002066156 cited in the application see the whole document -& DATABASE EMBL - EMHUM2 Entry HSU92436, Acc.No. U92436, 3 April 1997 STECK, P.A. ET AL.: "Human mutated in multiple advanced cancers protein (MMAC1) mRNA, complete cds." XP002066161 see the whole document	4-16, 18-20, 22,23, 25-28,41
X	PAYRASTRE, B. ET AL.: "Phosphoinositide 3-phosphatase segregates from phosphatidylinositol 3-kinase in EGF-stimulated A431 cells and fails to in vitro hydrolyse phosphatidylinositol(3,4,5)trisphosphate." FEBS LETTERS, vol. 341, 1994, pages 113-8, XP002088256 see the whole document	10,12
X	ZHOU, G. ET AL.: "The catalytic role of Cys124 in the dual specificity phosphatase VHR." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 269, no. 45, 11 November 1994, pages 28084-90, XP002088257 see the whole document	13,15, 16,22

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4

INTERNATIONAL SEARCH REPORT

Int tional Application No
PCT/US 98/14205

C (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
P,X	MYERS, M. ET AL.: "P-TEN, the tumor suppressor from human chromosome 10q23, is a dual-specificity phosphatse." PROC.NATL.ACAD.SCI.USA, vol. 94, August 1997, XP002088258 cited in the application see the whole document	4-23, 25-28
P,X	MAEHAMA, T. ET AL.: "The tumor suppressor, PTEN/MMAC1, dephosphorylates the lipid second messenger, phosphatidylinositol 3,4,5-triphosphate." JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 273, no. 22, 29 May 1998, pages 13375-8, XP002088259 see the whole document	4-16, 22-24, 33-35
E	WO 98 34624 A (UNIV COLUMBIA ;PARSONS RAMON E (US); COLD SPRING HARBOR LAB (US);) 13 August 1998 see the whole document	1-20, 22-28, 36-38, 41,44
E	WO 98 33907 A (MYRIAD GENETICS INC ;STECK PETER (US); JASSER SAMAR A (US); UNIV T) 6 August 1998 see the whole document	1-14, 18-20, 22-25, 27,28, 36-38, 41,44

4

INTERNATIONAL SEARCH REPORT

International application No
PCT/US 98/14205

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Remark : although claims 36-40,44 and 49-51, and 45-48 in as far as they relate to in vivo use, are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

SEE ADDITIONAL SHEET

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [X] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 98 14205

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1,3-9,11,12,36-38,42-44 and 10,12,24,33-35, 45-51 partially

Wild-type P-TEN, nucleic acid encoding it, antibodies against it, and their uses in the preparation of medicaments, methods of treatment and diagnosis.

2. Claims: 2,10,12,13-17,22-25,27-35,39-41 and 45-51, all partially

G129R mutein of P-TEN, nucleic acid encoding it, antibodies against it, and their uses in the preparation of medicaments, methods of treatment and diagnosis.

3. Claims: 2,10,12,13-17,22-25,27-35,39-41 and 45-51, all partially

H123Y mutein of P-TEN, nucleic acid encoding it, antibodies against it, and their uses in the preparation of medicaments, methods of treatment and diagnosis.

4. Claims: 2,10,12,13-15,22-25,27-35,39-41 and 45-51, all partially

M134L mutein of P-TEN, nucleic acid encoding it, antibodies against it, and their uses in the preparation of medicaments, methods of treatment and diagnosis.

5. Claims: 2,10,12,13,14,18-25,27-35,39-41 and 45-51, all partially

L57W mutein of P-TEN, nucleic acid encoding it, antibodies against it, and their uses in the preparation of medicaments, methods of treatment and diagnosis.

6. Claims: 2,10,12,13,14,18-25,27-35,39-41 and 45-51, all partially

G165R mutein of P-TEN, nucleic acid encoding it, antibodies against it, and their uses in the preparation of medicaments, methods of treatment and diagnosis.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

7. Claims: 2,10,12,13,14,18-25,27-35,39-41 and 45-51, all partially

T167P mutein of P-TEN, nucleic acid encoding it, antibodies against it, and their uses in the preparation of medicaments, methods of treatment and diagnosis.

8. Claims: 2,10,12,13,14,18-25,27-35,39-41 and 45-51, all partially

S170R mutein of P-TEN, nucleic acid encoding it, antibodies against it, and their uses in the preparation of medicaments, methods of treatment and diagnosis.

9. Claims: 2,10,12,13-17,22-25,27-35,39-41 and 45-51, all partially

G129E mutein of P-TEN, nucleic acid encoding it, antibodies against it, and their uses in the preparation of medicaments, methods of treatment and diagnosis.

10. Claims: 2,10,12,13-15,22-25,27-35,39-41 and 45-51, all partially

C124S mutein of P-TEN, nucleic acid encoding it, antibodies against it, and their uses in the preparation of medicaments, methods of treatment and diagnosis.

11. Claims: 2,13-16,18-20,22-35,39-41 and 45-51, all partially

Muteins of P-TEN other than those specified above, nucleic acids encoding them, antibodies against them, and their uses in the preparation of medicaments, methods of treatment and diagnosis.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 98/14205

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9715686 A	01-05-1997	AU 7316196 A	15-05-1997
		CA 2232241 A	01-05-1997
		EP 0859860 A	26-08-1998
		NO 981662 A	12-06-1998
WO 9834624 A	13-08-1998	AU 6653698 A	26-08-1998
WO 9833907 A	06-08-1998	AU 6018998 A	25-08-1998

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/22158

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/55 C12N9/16 C07K16/40 C12Q1/42 C12Q1/68
A61K38/46

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EMBL, EPO-Internal, WPI Data, BIOSIS, STRAND, MEDLINE, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	DATABASE EMBL 'Online! Accession number AI021222, 18 June 1998 (1998-06-18) MARRA, M. ET AL.: " ub03e08.r1 Soares mouse mammary gland NbMMG Mus musculus cDNA clone IMAGE:1365926 5' similar to TR:P91585 P91585 COS41.7. ; mRNA sequence." XP002159207 abstract relevant to invention 1 --- -/--	1-12, 18-23

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 May 2001	27.06.01

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Morawetz, R

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No
X	DATABASE SWALL 'Online! Accession number 043183, 1 June 1998 (1998-06-01) LI, L. ET AL.: "Tyrosine phosphatase CDC14B" XP002159208 abstract relevant to invention 1 -& LI, L. ET AL.: "A family of putative tumor suppressors is structurally and functionally conserved in humans and yeast." J. BIOL. CHEM, vol. 272, no. 47, 21 November 1997 (1997-11-21), pages 29403-29406, XP002159206 ---	1-12, 18-23
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X	MUDA MARCO ET AL: "Molecular cloning and functional characterization of a novel mitogen-activated protein kinase phosphatase, MKP-4" JOURNAL OF BIOLOGICAL CHEMISTRY,THE AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, INC.,,US, vol. 272, no. 8, 1997, pages 5141-5151, XP002144712 ISSN: 0021-9258 relevant to inventions 1, 6, 9, 10, 11, 12, 13, 14, 15, 16 ---	1-12, 18-23
X	DATABASE EMBL 'Online! Accession number AA023073, 10 August 1996 (1996-08-10) MARRA, M. ET AL.: " mh66e03.r1 Soares mouse placenta 4NbMP13.5 14.5 Mus musculus cDNA clone" XP002159242 the whole document relevant to invention 1 --- -/--	1-10

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	DATABASE EMBL 'Online! Accession number AA374753, 18 April 1997 (1997-04-18) ADAMS, M.D. ET AL.: "EST86937 HSC172 cells I Homo sapiens cDNA 5' end similar to similar to tyrosine phosphatase CL100." XP002167448 the whole document relevant to invention 6	1-12, 18-23
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X	DATABASE EMBL 'Online! Accession number AA461185, 13 June 1997 (1997-06-13) HILLIER, L. ET AL.: "zx70e02.s1 Soares_total_fetus_Nb2HF8_9w Homo sapiens cDNA clone IMAGE:796826 3' similar to WP:ZK757.2 CE00468 PROTEIN-TYROSINE PHOSPHATASE ; mRNA sequence." XP002167685 the whole document relevant to invention 9 abstract --- -/--	1-12, 18-23

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No
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X	DATABASE EMBL 'Online! Accession number AA723271, 8 January 1998 (1998-01-08) HILLIER, L. ET AL.: "zg88b02.s1 Soares_fetal_heart_NbHH19W Homo sapiens cDNA clone IMAGE:409611 3' similar to SW:DUS3_HUMAN P51452 DUAL SPECIFICITY PROTEIN PHOSPHATASE 3 ; mRNA sequence." XP002167684 the whole document relevant to invention 9 ---	1-12, 18-23
X	DATABASE EMBL 'Online! Accession number AA813372, 16 February 1998 (1998-02-16) STRAUSBERG, R:: "aj33b01.s1 Soares_testis_NHT Homo sapiens cDNA clone 1392073 3' similar to TR:Q93592 Q93592 F26A3.4. ; mRNA sequence." XP002167608 the whole document relevant to invention 10 ---	1-12, 18-23
X	DATABASE EMBL 'Online! Accession number AI025489, 19 June 1998 (1998-06-19) STRAUSBERG, R.: "ov67c10.x1 Soares_testis_NHT Homo sapiens cDNA clone IMAGE:1642386 3' similar to WP:F26A3.4 CE09669 PROTEIN-TYROSINE PHOSPHATASE ; mRNA seqeunce." XP002167609 the whole document relevant to invention 10 --- -/--	1-12, 18-23

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
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X	DATABASE EMBL 'Online! Accession number AA915932, 16 April 1998 (1998-04-16) STRAUSBERG, R.: " on18c06.s1 NCI_CGAP_Lu5 Homo sapiens cDNA clone IMAGE:1557034 3' similar to TR:Q91790 Q91790 MAP KINASE PHOSPHATASE ; mRNA sequence." XP002167451 the whole document relevant to invention 11 ---	1-12, 18-23
X	DATABASE EMBL 'Online! Accession number AC003072, 18 November 1997 (1997-11-18) MURRAY, J. ET AL.: " Human BAC clone CTA-963H5 from 22q12.1-qter, complete sequence." XP002167452 the whole document relevant to invention 11 ---	1-10
X	DATABASE EMBL 'Online! Accession number AA147450, 14 December 1996 (1996-12-14) HILLIER, L. ET AL.: "zl51g08.r1 Soares_pregnant_uterus_NbHPU Homo sapiens cDNA clone IMAGE:505502 5' similar to SW:PVH1_YEAST Q02256 PROTEIN-TYROSINE PHOSPHATASE YVH1 ; mRNA sequence." XP002167453 the whole document relevant to invention 12 --- -/--	1-12, 18-23

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	DATABASE EMBL 'Online! Accession number AA489562, 2 July 1997 (1997-07-02) HILLIER, L. ET AL.: "ab40g09.r1 Stratagene HeLa cell s3 937216 Homo sapiens cDNA clone IMAGE:843328 5' similar to SW:PVH1_YEAST Q02256 PROTEIN-TYROSINE PHOSPHATASE YVH1 ; mRNA sequence." XP002167454 the whole document relevant to invention 12 --- DATABASE EMBL 'Online!	1-12, 18-23
X	Accession number AA314946, 18 April 1997 (1997-04-18) ADAMS, M.D. ET AL.: "EST186775 HCC cell line (matastasis to liver in mouse) II Homo sapiens cDNA 5' end similar to similar to tyrosine phosphatase CL100." XP002167455 the whole document relevant to invention 12 --- DATABASE EMBL 'Online!	1-12, 18-23
X	Accession number AI264834, 16 November 1998 (1998-11-16) STRAUSBERG, R.: "qx66f03.x1 NCI_CGAP_Ov36 Homo sapiens cDNA clone IMAGE:2006333 3' similar to TR:Q91790 Q91790 MAP KINASE PHOSPHATASE ; mRNA sequence." XP002167456 the whole document relevant to invention 13 --- DATABASE EMBL 'Online!	1-12, 18-23
X	Accession number AI672432, 19 May 1999 (1999-05-19) STRAUSBERG, R.: "wa03b04.x1 NCI_CGAP_Kid11 Homo sapiens cDNA clone IMAGE:2296975 3' similar to TR:Q29449 Q29449 CHROMAFFIN GRANULE ATPASE II. ; mRNA sequence." XP002167457 the whole document relevant to invention 13 --- DATABASE EMBL 'Online!	1-10
X	Accession number AI018628, 18 June 1998 (1998-06-18) STRAUSBERG, R.: "ou47g09.x1 NCI_CGAP_Br2 Homo sapiens cDNA clone IMAGE:1631008 3' similar to TR:Q29449 Q29449 CHROMAFFIN GRANULE ATPASE II. ; mRNA sequence." XP002167458 the whole document relevant to invention 13 --- -/--	1-10

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
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A	-& DATABASE SWALL 'Online! Accession number Q39491, 1 November 1997 (1997-11-01) HARING, M.A. ET AL.: "DUAL SPECIFICITY PROTEIN PHOSPHATASE (EC 3.1.3.48) (EC 3.1.3.16)" XP002167613 the whole document --- -/--	

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Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	TANOUE TAKUJI ET AL: "Molecular cloning and characterization of a novel dual specificity phosphatase, MKP-5" JOURNAL OF BIOLOGICAL CHEMISTRY, AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, BALTIMORE, MD, US, vol. 274, no. 28, 9 July 1999 (1999-07-09), pages 19949-19956, XP002148678 ISSN: 0021-9258 the whole document relevant to invention 15	1-12, 18-23
X	-& DATABASE EMBL 'Online! Accession number AB026436, 28 June 1999 (1999-06-28) TANOUE, T. ET AL.: "Homo sapiens mRNA for dual specificity phosphatase MKP-5, complete cds." XP002167549 the whole document	1-12, 18-23

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	DATABASE EMBL 'Online! Accession number AF073482, 17 November 1998 (1998-11-17) LAPORTE, J. ET AL.: "Homo sapiens myotubularin related protein 7 mRNA, partial cds." XP002167553 the whole document relevant to invention 18 ---	1-12, 18-23
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Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
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A	WO 99 02704 A (MYERS MICHAEL P ;COLD SPRING HARBOR LAB (US); TONKS NICHOLAS K (US) 21 January 1999 (1999-01-21) the whole document relevant to inventions 1, 6 ---	
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Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
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A	DATABASE EMBL 'Online! Accession number AF038844, 6 January 1999 (1999-01-06) YUAN Y. ET AL.: "Homo sapiens MKP-1 like protein tyrosine phosphatase mRNA, complete cds." XP002167460 the whole document relevant to invention 13 ---	
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication where appropriate, of the relevant passages	Relevant to claim No
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A	DATABASE SWALL 'Online! Q13613, 1 November 1997 (1997-11-01) KIOSCHIS, P. ET AL.: "MYOTUBULARIN-RELATED PROTEIN 1 (FRAGMENT)." XP002167556 the whole document relevant to invention 17	
P,X	DATABASE EMBL 'Online! Accession number AW258860, 26 December 1999 (1999-12-26) MARRA, M. ET AL.: "um74f03.y1 Sugano mouse kidney mkia Mus musculus cDNA clone IMAGE:2300957 5' similar to TR:P91585 COS41.7; mRNA sequence" XP002159210 abstract relevant to invention 1	1-12, 18-23
P,X	WO 00 06728 A (INCYTE PHARMA INC ;PATTERSON CHANDRA (US); AZIMZAI YALDA (US); COR) 10 February 2000 (2000-02-10) see SEQ ID NO: 27, SEQ ID NO: 58 for invention 6 and SEQ ID NO: 11, SEQ ID NO: 42 for invention 9 relevant to inventions 6, 9	1-12, 18-23
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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(54) Title: NOVEL PROTEIN PHOSPHATASES AND DIAGNOSIS AND TREATMENT OF PHOSPHATASE-RELATED DISORDERS

(57) Abstract: The present invention concerns polypeptides, nucleic acids encoding such polypeptides, cells, tissues and animals containing such nucleic acids, antibodies to the polypeptides, assays utilizing the polypeptides, and methods relating to all of the foregoing. Preferably, the polypeptides of the present invention are phosphatases. Through the use of a "motif extraction" bioinformatics script, additional mammalian members of the phosphatase family are herein presented. These phosphatases include MKP-like proteins, a CDC14-like protein, a PTEN-like protein, and myotubularin (MTM)-like proteins. Classification of proteins as new members of established families has proven highly accurate not only in predicting motifs present in the remaining non-catalytic portion of each protein, but also in their regulation, substrates, and signaling pathways.